

Atty. Dkt. No. 078853-0302

**Amendments to the Claims**

1. (Currently amended) A method for treating or preventing cardiovascular or cerebrovascular disease in a mammal, comprising administering an agent that alters the activity or concentration of an enzyme, wherein said enzyme catalyzes a reaction that produces or degrades a sphingolipid or a sphingolipid metabolite.

2. (Original) A method for treating or preventing undesirable post-ischemic events in an animal, comprising administering thereto an agent that alters the activity or concentration of an enzyme, wherein said enzyme catalyzes a reaction that produces or degrades a sphingolipid or a sphingolipid metabolite.

3. (Original) The method of claim 2 wherein said undesirable post-ischemic events occur in the heart.

4. (Original) The method of claim 2 wherein said undesirable post-ischemic events occur in the brain.

al 5. (Currently amended) A method for treating or preventing cardiovascular disease in a human, comprising administering an agent that alters the activity or concentration of an enzyme, wherein said enzyme catalyzes a reaction that produces or degrades a sphingolipid or a sphingolipid metabolite.

6. (Original) The method of claim 5, wherein said sphingolipid or a sphingolipid metabolite is selected from the group consisting of sphingomyelin, sphingosine, S-1-P, ceramide, SPC, 3-ketosphinganine, galactosylceramide and dihydroceramide.

7. (Original) The method of claim 5, wherein said enzyme is selected from the group consisting of SM synthase, SM deacylase, SMase, ceramidase, S-1-P phosphatase, SPH kinase, Cer synthase, S-1-P lyase, cerebrosidease, Cer-1-P phosphatase, Cer kinase, SM deacylase, SPT, NADPH-dependent reductase.

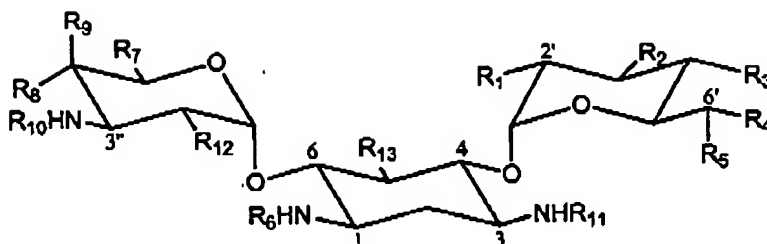
8. (Original) The method claim 5, wherein said enzyme is SMase.

9. (Original) The method claim 8, wherein said agent is an aminoglycoside.

10. (Original) The method claim 9, wherein said aminoglycoside is a gentamicin.

11. (Original) The method claim 9, wherein said agent that inhibits SMase has the structure

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wherein:

each of R1-R13 is independently hydrogen, alkyl, optionally substituted alkyl, alkenyl, optionally substituted alkenyl, alkynyl, optionally substituted alkynyl, aryl, optionally substituted aryl, cycloalkyl, optionally substituted cycloalkyl, alkoxy, optionally substituted alkoxy, heterocyclic, optionally substituted heterocyclic, heteroaryl, optionally substituted heteroaryl, hydroxyl, halogen, nitro, carboxyl, thioalkyl, amino, alkylamino, arylamino, amido, ammonium, alkylammonium, sulfonyl, aminosulfonyl, alkylsulfonyl, alkoxycarbonyl, acetyl, or acyl.

12. (Original) The method claim 11, wherein:

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each of R1-R13 is independently hydrogen, alkyl, optionally substituted alkyl, alkenyl, optionally substituted alkenyl, alkynyl, optionally substituted alkynyl, alkoxy, optionally substituted alkoxy, aryl, optionally substituted aryl, cycloalkyl, optionally substituted cycloalkyl, heterocyclic, optionally substituted heterocyclic, heteroaryl, optionally substituted heteroaryl, hydroxyl, halogen, nitro, carboxyl, thioalkyl, amino, alkylamino, arylamino, amido, ammonium, alkylammonium, sulfonyl, aminosulfonyl, alkylsulfonyl, alkoxycarbonyl, acetyl, or acyl,

with the proviso that when R6 = H, R7 = H, R8 = CH3, R9 = OH, R10 = CH3, R11 = H, R12 = OH, and R13 = OH,

if R1 = NH2, R2 = H, R3 = H, and R4 = CH3, then R5 is not NH2 or NHCH3,

and if R1 = OH, R2 = OH, R3 = OH, and R4 is H, then R5 is not NH2.

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13. (Original) The method claim 11, wherein:

R1 = NH<sub>2</sub>,  
R2 = H,  
R3 = H,  
R4 = CH<sub>3</sub>,  
R5 = NH<sub>2</sub> or NHCH<sub>3</sub>,  
R6 = H,  
R7 = H,  
R8 = CH<sub>3</sub>,  
R9 = OH,  
R10 = CH<sub>3</sub>,  
R11 = H,  
R12 = OH, and  
R13 = OH.

14. (Original) The method claim 11, wherein:

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R1 = OH,  
R2 = OH,  
R3 = OH,  
R4 = H,  
R5 = NH<sub>2</sub>,  
R6 = H,  
R7 = H,  
R8 = CH<sub>3</sub>,  
R9 = OH,  
R10 = CH<sub>3</sub>,  
R11 = H,  
R12 = OH, and  
R13 = OH.

15. (Original) The method of claim 1, wherein said disease is a cardiovascular disease.

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16. (Original) The method of claim 15, wherein said cardiovascular disease is a cardiac disease.

17. (Original) The method of claim 16, wherein said cardiac disease is selected from the group consisting of myocardial ischemia; acute myocardial infarction (AMI); coronary artery disease (CAD); acute coronary syndrome (ACS); cardiac cell and tissue damage that may occur during or as a consequence of percutaneous revascularization (coronary angioplasty) with or without stenting; coronary bypass grafting (CABG) or other surgical or medical procedures or therapies that may cause ischemic or ischemic/reperfusion damage; and cardiovascular trauma.

18. (Original) A pharmaceutical composition comprising an agent that modulates the activity of an enzyme that catalyzes a reaction that produces or degrades a sphingolipid or a sphingolipid metabolite.

a 19. (Original) A method for treating or preventing cardiovascular or cerebrovascular disease, comprising administering the pharmaceutical composition of claim 18.

20. (Original) A formulation comprising an agent which will, when provided to an animal in need thereof, alter the activity or concentration of an enzyme that produces or degrades a sphingolipid or a sphingolipid metabolite to a degree necessary to achieve a therapeutic effect.